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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/431,888	11/02/1999	Lyn M. Wise	1064/44803	9374

7590

05/07/2002

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EXAMINER

ANDRES, JANET L

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 05/07/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/431,888

Applicant(s)

WISE ET AL.

Examiner

Janet L Andres

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 53-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 2-6, 55 and 56 is/are allowed.
- 6) ☒ Claim(s) 1, 7 and 53 is/are rejected.
- 7) ☒ Claim(s) 54 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 February 2002 has been entered.

Claims 1-7 and 53-56 are pending in this application.

Claim Rejections - 35 USC § 103

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1, 7, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lyttle et al. cited in previous office actions, in view of Thomas, cited in previous office actions.

Applicant argues that Lyttle et al. does not suggest that the observed activity was due to a viral protein and states that Lyttle et al. suggest that the activity was due to a "VEGF-like gene" and that Lyttle et al. states that the reason for the activity was not clear. Applicant further argues that what is demonstrated by Lyttle et al. is activity in cell supernatants, and that Lyttle et al. refers to unpublished data. Applicant additionally argues that the activity might be due to another factor, not necessarily viral in nature. Applicant further argues that the activity, even if due to the VEGF protein, might require post-translational modification. Applicant concludes that the teachings of Lyttle et al. in view of those of Thomas do not provide a reasonable expectation of success, and at most indicate that it was only "obvious to try" Applicant's claimed

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invention. Applicant additionally points to the publication of Applicant's results in the Proceedings of the National Academy of Sciences as evidence of Applicant's invention.

Applicant's arguments have been fully considered but have not been found to be persuasive.

Lyttle et al. states in the abstract that "it is likely that this activity is due to the expression of the VEGF-like gene". One of ordinary skill in the biochemical arts would assume that it was the protein, not the mRNA, to which the authors referred. That RNA is translated into protein, that the protein is post-translationally modified, and that the protein binds to a receptor, resulting in biological activity is the normal and expected mechanism by which growth factors function. Thomas also specifically teaches VEGF as a "homodimeric glycoprotein" (p. 603) and discusses the biochemical characteristics of VEGF proteins in detail. Thus, one of ordinary skill in the art would expect, on reading that Lyttle et al. believed the activity to be due to a VEGF gene, that it was the expressed protein that actually had the activity. The mitogenic activity of the supernatants taken with Lyttle et al.'s specific suggestion that the VEGF-like protein was responsible and what is known about VEGF, further provide a sufficient expectation of success. The VEGF family and its activities are well known and those activities are highly characteristic. Thomas states that VEGF is "the most selective vascular endothelial cell mitogen known" (p. 605). Thus the artisan of ordinary skill, on learning that the supernatants of cells containing a virus with a VEGF-like gene were mitogenic for vascular endothelial cells as compared to control cells, would readily expect that Lyttle et al. were correct in their assertion that the VEGF-like gene product was responsible for the activity. Applicant's PNAS publication is not evidence that the finding was unexpected. The standards for publication are not those of patentability, and

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the paper further contains additional information concerning NZ-7 and the receptor-binding characteristics of the two proteins that is not obvious from the teachings of Lyttle et al. and Thomas.

Applicant additionally argues that the interaction of ORFV2-VEGF with VEGFR2 is not obvious. This argument is found persuasive and this basis of the rejection, and thus the rejection of the claims to which it applies, is withdrawn. While there is evidence in the literature to suggest that VEGFR2 is responsible for the mitogenic activities of VEGF, there was considerable doubt as to the roles of the various receptors at the time of filing. Thus the ability of a VEGF analogue to stimulate vascular endothelial cell proliferation would not have indicated to one of ordinary skill that it did so through VEGFR2. One of ordinary skill would further not have expected that the protein would not bind to VEGFR1.

Thus, it would be obvious to one of ordinary skill in the art to combine the teachings of Lyttle et al. with those of Thomas to use ORFV2-VEGF to stimulate the proliferation of endothelial cells. One of ordinary skill would have been motivated to do so because Lyttle et al. teaches that this protein is a VEGF homologue and that cell supernatants from cells infected with the ORFV2 virus have VEGF-like activity, and further because Thomas teaches such activities for VEGF. It would not have been obvious, however, to use this protein to activate the VEGF receptor 2; this interaction would not have been obvious from the mitogenic activity of ORFV2-VEGF. Further, it would not have been obvious to use NZ10, since Lyttle et al. do not teach or suggest this protein. Thus claims 1, 7, and 53, which encompass stimulation of VEGF functions by ORFV2-VEGF, are rejected. Claims 2-6, 55, and 56, which encompass only NZ10 or require interaction with VEGF receptor 2, are not obvious over Lyttle et al. in view of Thomas.

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Claim Objections

4. Claim 54 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

CLAIMS 1, 7, AND 53 ARE REJECTED. CLAIMS 2-6, 55, AND 56 ARE ALLOWED. CLAIM 54 IS OBJECTED TO.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly

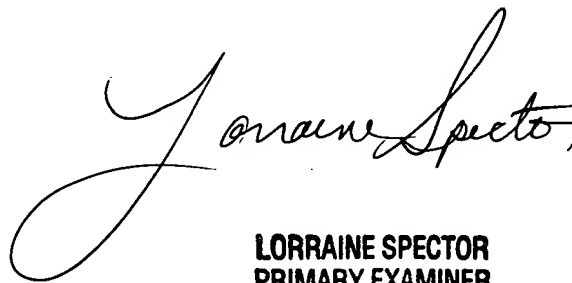
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set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.

May 6, 2002



LORRAINE SPECTOR
PRIMARY EXAMINER